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MEDICAL EFFECTS OF COCAINE/CRACK

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MEDICAL EFFECTS OF COCAINE/CRACK

Prepared for the

Alberta Family Life and Substance Abuse Foundation

by
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SUMMARY

Cocaine continues to be an important drug--both because of its continued popularity as a "street" drug and because of the significant dangers associated with its use.

Cocaine can be: sniffed (snorted) into the nose, injected intravenously (IV), smoked, or taken orally.

Crack is a form of cocaine that can be smoked. Smoking cocaine produces a rapid, dramatic effect without the dangers of injecting associated with intravenous use. These effects, plus availability in small, inexpensive amounts, have contributed to crack's popularity.

MEDICAL EFFECTS OF COCAINE/CRACK

Dose

Usual oral doses of cocaine range from 100 to 200 mg, intravenous doses, 25 to 50 mg and smoked doses, 250 to 1000 mg. Very heavy users may sniff or smoke up to 10 grams (10,000 mg) per day, although most users take much less.

The dose of cocaine that causes the different medical effects varies greatly from one individual to another. While dramatic effects have resulted from doses as small as a few hundred mg, many users commonly take much larger doses. Since the non-medical use of cocaine involves large doses that have never been studied in experimental conditions, the amounts causing various medical effects are not known.

Addictive Potential

Contrary to earlier information and the belief of many users, cocaine does produce addiction/drug dependence, causing both tolerance and withdrawal. Crack and other smoked forms of cocaine are at least as addictive as intravenously injected drugs.

Cocaine/Crack Babies

Dramatic media reports about cocaine/crack babies are not supported by the available scientific information. The effects of cocaine use--on the growth and development of the fetus/infant, or in producing fetal abnormalities and withdrawal following birth--are not well established.

Cocaine use does increase complications during pregnancy such as spontaneous abortions and premature birth.

Cardiovascular Effects

Serious cardiovascular complications can result from cocaine use. They include: heart attacks, strokes, abnormal heart rhythms, other heart muscle abnormalities, and death.

Strokes are a serious complication of cocaine use that can occur after any route of administration.

Effects on the Respiratory System

Cocaine smoking may lead to chronic lung damage particularly in habitual smokers. Crack probably does not cause any more serious effects than other forms of smoked cocaine.

Infants and toddlers have experienced serious adverse effects, including seizures, when exposed to high levels of second hand cocaine smoke.

Repeated, heavy cocaine sniffing or snorting can cause severe injury to the inner surfaces of the nose and result in perforation of the nasal septum which divides the two nasal passages.

Effects on the Nervous System

Seizures are one of the more common complications of cocaine use. People with a history of epilepsy are probably at greatest risk, however seizures have been reported in otherwise normal people, and they are commonly associated with death resulting from cocaine use.

Chronic, heavy use of cocaine probably causes some diffuse brain damage. Further research is necessary to determine the extent of damage and the amount of impairment that results.

Psychiatric Effects

While depression is a major symptom of cocaine withdrawal, self-medication of depression may be a reason for cocaine use.

Varying degrees of severe psychiatric disorders, including paranoid psychosis, occur not uncommonly in chronic, heavy cocaine users.

Other Medical Effects

Cocaine causes immune system depression, but the importance remains to be clarified. One study has shown that use of drugs such as alcohol and cocaine may not effect the development of disease in HIV positive men.[1] However, it would seem wise for those with HIV infection/AIDS or other causes of immunodeficiency to avoid or at least limit use of intoxicants that have the potential to further depress the immune system.

Cocaine use can result in: allergic reactions, dangerously high body temperatures, serious stomach and intestinal complications, liver damage, impaired sexual function, and muscle wasting.

Reports of death related to cocaine use have increased significantly during the past decade. Death is usually rapid and unpredictable; and has occurred with all routes of administration and at a wide range of doses.

Indirect medical effects can result from cocaine use. Serious burns and injuries occur when solvents used in preparing free-base cocaine explode. Infections such as hepatitis and AIDS and other complications can result from injecting illicit drugs with non-sterile equipment. S.T.D.'s , including syphilis and AIDS, can be contracted during the exchange of sex for drugs.

Despite the wide range of toxic effects of cocaine outlined in this review, apparently, many users still consider it a relatively safe, non-addictive drug. This is unfortunate, since medically cocaine is by no means a safe drug, and it definitely can produce addiction.

INTRODUCTION

Epidemiology

Cocaine continues to be one of the more commonly used "street" drugs. In Canada in 1989, 1.4% of people 15 years of age and older reported using cocaine at least once in the past year.[2] For Alberta the figure was 1.1%. More recently, in 1991 in Ontario, 1.6% of high school students and 1.8% of adults reported use in the past year.

More disturbing are the Ontario results that 64% of street kids used cocaine in the past year, 6% used it daily; and 39% of street kids used crack in the year, 6% reporting daily use.[3]

Problems associated with heavy cocaine use are a particular concern. Although the overall use of cocaine has been decreasing over the past several years, U.S. data show that heavy users represent a greater proportion of all users and appear to be developing greater problems. According to the Drug Abuse Warning Network (DAWN) in the U.S., there was a fivefold increase in the number of emergency room visits by people using cocaine and a 28-fold increase in the number of visits by smokers of cocaine in 1988 compared to 1984.[4]

These data support the need for a thorough review of the medical effects of cocaine. This is particularly true since many users still assume that cocaine is a safe, non-addicting drug.

Effects of Cocaine

Cocaine is a powerful nervous system stimulant that has direct or indirect effects on many body systems.

The effects of intoxication with cocaine vary greatly depending on: the amount of drug and how it is taken, the user's expectations, and the setting in which the drug is taken. An intense feeling of euphoria and well-being is most desired by the user. Other effects can include: alertness, decreased appetite and need for sleep, and feelings of enhanced energy.

Less desired effects such as severe agitation, assaultive behavior, paranoid thoughts, delirium, and fainting can also occur. Undesirable physical effects may include: nausea, vomiting, chest pain, tremors, seizures, high temperature, high blood pressure, respiratory arrest, abnormal heart rhythms and death.

The first major medical report on the effects of cocaine, On Coca, was published in 1884 by Sigmund Freud. He recognized the local anesthetic effects, but was more interested in it as a stimulant. Freud probably created the first modern cocaine addict when he tried it as a treatment for a patient addicted to morphine.

Cocaine is still used as a local anesthetic but only for surface anesthesia in ear, nose, and throat surgery. It has the unique advantage of producing constriction of blood vessels as well as local anesthesia. The result is less operative bleeding and better surgical visualization.

Dose

The doses of cocaine used depend on factors such as the purity, the route of administration, and the degree of tolerance the user has developed. A common pattern among users in social settings involves sniffing ("snorting") into each nostril 20-30 mg of cocaine powder that has been finely chopped with a razor blade and arranged into "lines": thin strips about 0.3 cm wide and 2.5 cm long. This amount may be repeated two or three times an hour over several hours.

Usual oral doses range from 100 to 200 mg, intravenous doses, 25 to 50 mg, and smoked doses, 250 to 1000 mg. Very heavy users may sniff or smoke up to 10 grams (10,000 mg) per day, although most users take substantially less.

Source

Cocaine comes from the plant Erythroxylum coca and related species.[5] These South American shrubs, when cultivated, are maintained at a height of 3 to 4 ft., and grow primarily in the Andes mountains of Bolivia and Peru, although they are also now being grown in Columbia.

Since at least 1500 B.C., the Andean Indians have chewed the leaves of these plants. The resulting mild stimulant effect is very different from the marked stimulant and euphoric effects produced by snorting, smoking, or injecting the purified cocaine.

Cocaine is removed from the leaves of the coca plant using a series of extractions with: sulphuric acid, lime water, gasoline, more acid, potassium permanganate, and ammonia. Coca paste is the resulting partly purified product from which cocaine can then be isolated.

Cocaine Preparations

Cocaine is usually available as the salt, cocaine hydrochloride, a white powder which is either snorted directly into the nose, or dissolved in water and injected.

Free base (cocaine base) is a form of cocaine prepared by heating cocaine hydrochloride salt with various liquids. Free base--cocaine with the hydrochloride removed--is more volatile and chemically stable than the salt, so can be smoked. The danger in preparing free base is that the liquids (solvents) used are very flammable and explosions can result.

Crack, another form of free base, is made by heating cocaine hydrochloride with baking soda. The mixture forms a sold chunk composed of chemicals that includes free base cocaine. It is divided into many tiny "rocks" that are sold for $15 or $20 or less. As crack, cocaine becomes available in small but more affordable amounts.

The appeal of crack and other types of free base cocaine is that they can be smoked. Inhalation of the smoke produces a slightly more rapid and possibly even more dramatic effect than when the drug is injected. Also, it circumvents the need to inject and avoids the associated complications, in particular, the possibility of transmitting: infections such as hepatitis, and HIV the virus that causes AIDS.

Common street names for cocaine include: coke, C, snow, flake, blow, speedball (cocaine and heroin), free base, and crack.

1. ADDICTIVE POTENTIAL

As recently as the early 1980's, some references stated that cocaine use did not cause addiction.[6,7] This belief, still held by many cocaine users, has been suggested as one reason for the current popularity of cocaine as an intoxicant.

To help clarify this important subject, addiction will first be discussed in general terms, then the specific addictive potential of crack and cocaine will be considered.

1.1 Addiction

Addiction can be defined as a condition (social, psychological, and biological) where drug use becomes the most important activity in a persons life. The person continues to use the drug although it may be causing serious problems with: family relationships, employment, and mental and physical health.

To avoid the related moral overtones and vagueness, the term "addiction" is often replaced with the term "drug dependence" in the discussion of substance abuse. It is, however, commonly used in media reports and will be used here to avoid confusion in the discussion of specific aspects of dependence.

The "classic" concept of addiction includes: tolerance, withdrawal, and dependence. Tolerance is the need for more and more drug to produce the desired effect and withdrawal is the effect experienced when the drug is stopped. Dependence is a term used to describe the need for (dependence on) a drug.

The classic model includes two types of dependence. Physical dependence: withdrawal results in physical effects such as sweating and increased blood pressure. Psychological dependence: only psychological symptoms and craving for the drug follow withdrawal. In this model a drug is considered to be addictive if physical dependence occurs during withdrawal.

Studies of drugs such as cocaine have lead to some changes in this "classic" model. While few physical effects occur during the withdrawal from cocaine, psychological symptoms--loss of pleasure (anhedonia), depression, and low energy--are severe, and as a result extreme craving for the drug occurs.

It is now believed that these "psychological" symptoms have a physiological or physical basis.[8] As a result, the World Health Organization has discarded the old terms, physical and psychological dependence, for the more precise term "neuroadaptation". Thus, addiction is defined as drug use that produces neuroadaptation, which means that significant withdrawal will occur when the drug is stopped--an important factor causing the person to continue use of the drug.

In the past, it was also believed that tolerance did not develop with repeated cocaine use. There is now good evidence that this is not true[9]; further evidence that cocaine does produce addiction/drug dependence.[10]

1.2 Crack

Although media reports often imply that crack is a terribly addictive new drug, it is just another form of cocaine. However, as a form of free-base cocaine, crack can be smoked, and the inhaled drug reaches the brain very rapidly and produces a dramatic, but short lasting, euphoria, followed by an extreme low ("crash"). This sequence favors repeated use of the drug which can quite quickly result in addiction.

Crack is probably as addictive as intravenously injected cocaine which causes similar effects.[11] One difference with crack: it is sold in smaller, thus less expensive, amounts, so is available to more users.

1.3 Cocaine

As indicated in the discussion of addiction above, cocaine (including free-base forms such as crack) is an addictive drug. It is considered by many to be one of the most addictive of all drugs of abuse.[12]

However, instant addiction to cocaine does not occur. In fact, recent studies have shown that the majority of people who try cocaine never become addicted.[13] If the user progresses from intranasal use to smoking or injecting there is a much greater risk of addiction developing. For the 5 to 10% of users that do become addicted, cocaine is a particularly difficult drug to stop using.[14]

Animal studies give an indication of how powerful the urge to continue using cocaine is. Given free access to intravenous cocaine, animals will continue repeated drug use at the exclusion of eating or sleeping until they finally die.

The pattern of use differs for cocaine than for most other drugs. The cocaine dependent person does not consistently take their drug daily like the alcoholic or narcotic addict. They will go on binges or "sprees", lasting for hours or even days, usually until the supply of cocaine is used up, then will be abstinent for at least several days.

1.4 Withdrawal

The dependent person experiences a withdrawal that is also quite different from that produced by other drugs. A three phase pattern occurs.[15]

Phase one, the "crash", follows the end of the cocaine binge when the user has very low energy and mood, will sleep for several days and eat large amounts of food. This phase lasts for up to four days.

Phase two, "withdrawal", is similar to withdrawal from other drugs except for the absence of physical symptoms. During this phase which lasts for 2 to 12 weeks, the user feels little initiative to do things, intense boredom, and minimal pleasure from life. This limited existence compared to the memories of drug-induced euphoria induces severe craving, and can result in resumption of cocaine use, and unceasing cycles of recurrent binges.

Phase three, "extinction", gradually follows if no drug is taken for many months. Normal function returns, and eventually craving decreases or at least is not associated with a relapse to drug use.

2. COCAINE/CRACK BABIES

Babies born to mothers who used cocaine during pregnancy are often represented in the lay press as so severely brain damaged that they may never function normally in society. Titles in medical journals such as "Cocaine Babies: The Scourge of the '90s"[16], often based on reports of events only possibly related to cocaine use, reflect a similar bias. Critical review of the available information, while not denying the potential impact of cocaine use by pregnant women, does not support these extreme views.

In addition to possible effects on growth and development, cocaine use during pregnancy has been implicated in causing: fetal abnormalities, complications during pregnancy, and withdrawal following birth.

2.1 Growth and Development

Although a number of studies have indicated negative effects of cocaine exposure on fetal growth--as indicated by decreased birth weight and head circumference--many other factors such as use of other drugs, and poor nutrition could be contributing factors.[17]

Impairment in language development and motor skills have also been reported in children who were exposed to cocaine before birth. However, again it is very difficult to determine the effects of poverty, violence, abandonment, and inadequate or abusive parenting.

The current literature on the subject has recently been described as "far too slim and fragmented to allow any clear predictions about the effects of intrauterine exposure to cocaine on the course and outcome of child growth and development"[18].

In a 1992 editorial in the Journal of the American Medical Association, the authors of that assessment, recommend a well reasoned approach:

> ". . . suspension of judgment about the developmental outcome of cocaine-exposed babies until solid scientific data are available. Whatever the damage from prenatal exposure to cocaine may prove to be, outcome will not be improved by an attitude that assumes that exposed children cannot be helped or that they are different from other children."

2.2 Fetal Abnormalities (teratogenic effects)

A variety of abnormalities have been reported in babies born to mothers who used cocaine during pregnancy. To date, however, no specific abnormalities can be reliably attributed to cocaine use, and no specific "fetal cocaine syndrome" has been identified. Many of the difficulties associated with the study of the effects of alcohol on the fetus apply to cocaine.[19] In particular other drugs and environmental factors may have caused associated abnormalities.[20]

Many of the cocaine-associated anomalies involve the genital and urinary tracts, in particular, the testis and kidneys. Other associated abnormalities have involved the: heart and blood vessels, the brain, the face, the intestines, and the extremities.[21]

As for the association between cocaine use and impaired growth and development, there is a need for additional well designed studies to clarify the possible effects of cocaine use in producing fetal abnormalities. This is of particular importance, since one recent study (meta-analysis) of many of the human reports found no significant effect.[22]

2.3 Complications During Pregnancy

Cocaine users are more likely to have a variety of obstetrical complications during pregnancy than nondrug users.[23] These include: spontaneous abortions, premature separation of the placenta (abruptio placentae), and preterm labor and/or delivery. Transient cocaine-induced increases in blood pressure can also occur and be misinterpreted as a complication of pregnancy.

2.4 Withdrawal Following Birth

Withdrawal symptoms including: irritability, restlessness, and sleep problems, are well documented in babies born to mothers dependent on narcotics. While similar symptoms have been reported in babies of cocaine users by some workers[24], others have found no difference between cocaine exposed and nonexposed infants[25].

If withdrawal does occur in babies exposed to cocaine alone, it is apparently less severe than in those exposed to narcotics such as heroin or methadone. However, infants exposed to both heroin and cocaine have shown the most severe withdrawal symptoms.[26]

In addition to specific withdrawal symptoms, several early studies indicated a possible association between cocaine exposure and an increased incidence of unexplained sudden death in babies (sudden infant death syndrome, SIDS). A larger more recent study, however, did not confirm these findings.

3. CARDIOVASCULAR EFFECTS

The most common and serious medical complications of cocaine abuse involve the heart and blood vessels (cardiovascular system). They include: heart attacks, strokes, abnormal heart rhythms, and other heart muscle abnormalities.

At least some of the dramatic sudden deaths in apparently healthy celebrity figures such as the basketball star Len Bias result from the effects of cocaine on the cardiovascular system. Heart and blood vessel complications are second only to nervous system effects as a cause of cocaine-related deaths; in the case of strokes, both systems are affected.[27]

3.1 Heart Attacks

Of the cardiovascular complications of cocaine use, heart attacks are the most frequently reported . Up to 1992, 91 cases had been reported in the literature.[28] Of these, three patients died.

The patients were young (average age 32.8 years), and most were regular tobacco smokers (87%). All three common routes of administration were reported; not infrequently there was a history of prior episodes of chest pain, particularly following cocaine use. In fact, unexplained chest pain or heart attack in a young person is now considered a possible indication of cocaine abuse.

Although heart attacks occur most frequently soon after cocaine use, they have also been reported during withdrawal. They occur in people with underlying heart disease but also in people with no heart problems.

3.2 Strokes

See: Section 5.3 Nervous system: Other effects

The sudden, dramatic increase in blood pressure produced by cocaine, in addition to causing strokes (bleeding and rupture of blood vessels in the brain), can result in other catastrophic events including rupture of major arteries such as the aorta.[29]

3.3 Heart Rhythm Abnormalities

Increased heart rate is an immediate effect of cocaine injestion on the rhythm of the heart. Conversely, the heart can slow or even stop, or it can beat so fast that it ceases to pump effectively (fibrillation).

Abnormal heart rhythms may result from cocaine-induced heart attacks or other heart muscle damage, or from the direct effects of cocaine on the heart muscle. Other possible causes include: effects on nervous system transmitters (eg: noradrenalin); and the high temperature, seizures, and acidosis (high body acid levels) that can result from cocaine use.[30]

3.4 Heart Muscle Abnormalities

Cases of inflammation of the heart muscle (myocarditis) and other heart muscle disease (cardiomyopathy) have been associated with cocaine use. These, not common occurrences, may result from the direct effects of cocaine or of contaminants that are frequently added to street drugs. Inflammation which first occurs in the blood vessels, then in the heart muscles, may lead to generalized disease of the heart that seriously impairs its function.[31] Inflammation may also be caused by viral infections for which intravenous drugs users are at high risk.

4. EFFECTS ON THE RESPIRATORY SYSTEM

The effects of cocaine on the respiratory system depend on how the drug is used. Most complications, involving the lungs directly, occur when crack or other free base cocaine is smoked, because the material is inhaled directly into the lungs. There is no indication to date that crack causes any more serious effects than other forms of free base cocaine.

Many of the respiratory complications are the result of chronic cocaine abuse. However, acute intoxication by any route of administration can cause respiratory failure and death.

Snorting cocaine powder causes damage in the nose and adjacent areas of the upper respiratory tract due to high concentrations of cocaine deposited in these areas. Pulmonary complications related to injecting cocaine tend to result more from injecting than from the drug.

4.1 Lungs

Possible effect of cocaine on the lungs include: bleeding, build-up of fluid (pulmonary edema), rupture of air sacs, asthma, diffuse lung disease, lung infections, and long-term problems in the ability of the lung to exchange gases (carbon dioxide and oxygen).[32]

The pulmonary symptoms of cocaine use include: shortness of breath, cough, wheezing, coughing up blood (hemoptysis), and chest pain.[33]

Bleeding in the lungs is a fairly common complication of both cocaine snorting and smoking. Although usually not serious enough to require treatment, more serious lung injury has been reported to be responsive to corticosteroid drugs. Pulmonary edema (fluid build-up), on the other hand, is apparently rather rare, but in a young person with unexplained symptoms, cocaine abuse should be considered.

Rupture of an air sac is another fairly rare complication most often associated with smoking crack and other forms of free base cocaine. It usually occurs when the smoker applies pressure on the lungs while holding their breath (Valsalva maneuver), in an attempt to enhance drug absorption. Spontaneous recovery usually occurs: the rupture seals, and the air that escaped around the lungs (pneumothorax) and heart (pneumopericardium) is reabsorbed. Smoking cocaine has also been reported to cause severe, even life-threatening asthma attacks.

Recurring pneumonia-like symptoms, of severe chest pains, breathing problems and high temperatures following crack smoking in one patient, have been given the name "crack lung".[34] It is not known how commonly it occurs, or whether it is unique to crack, but several other cases of similar symptoms suggest that heavy cocaine smoking can cause acute, generalized lung disease.

Cocaine-related respiratory infections are usually associated with IV use, and result from infection at the injection site spreading to the lungs.

A number of reports relate chronic cocaine use, particularly smoking, to impairment of the lungs ability to exchange oxygen and carbon dioxide. Although other factors such as tobacco and marihuana smoking may contribute, this impairment may be due to intense constriction of blood vessels in the lung, decreased blood flow, and resulting chronic lung damage.

4.2 Nose and Adjacent Areas

Repeated, heavy sniffing or snorting of cocaine may cause severe injury and\or infection of the surfaces of the nasal passages (mucosa) and the nasal sinuses. The extreme constriction of the blood vessels may result in chronic sinus infections and perforation of the nasal septum which divides the two nasal passages.

Candidates for nasal surgery (rhinoplasty) are carefully screened for a history of chronic cocaine use, as surgery may not be possible, particularly if they are likely to continue drug use.

4.3 Other Respiratory Effects

Although not reported to cause specific lung problems, passive cocaine inhalation by infants and toddlers exposed to crack and other cocaine free base smoke has resulted in serious adverse effects. In one report two children experienced drowziness and unsteadiness of gait and two others had unexplained seizures following intense exposure to cocaine smoke.[35]

No reports were found relating cocaine use, smoked or taken by another route, to lung cancer. This is not that surprising as cocaine smokers inhale a more pure drug without the tar and many other compounds in smoked drugs such as tobacco and marihuana. The subject remains of interest.

5. EFFECTS ON THE NERVOUS SYSTEM

Cocaine has a variety of actions on the nervous system. The stimulant effect and euphoria result from complex effects on nervous system chemicals (neurotransmitters) in the brain, such as: dopamine, and serotonin. The local anesthetic effect results from a direct action to block the transmission of impulses along nerve fibres.

Cocaine affects neurotransmitters in other parts of the body in addition to those in the brain. The effects on stimulant parts of the peripheral nervous system (sympathethic nervous system) are of special importance. By blocking the removal (reuptake) of noradrenalin at the synapses where nerve endings meet, cocaine causes an increased activity of this part of the nervous system.[36] Results include: heart rate and blood pressure increases and constriction of blood vessels--actions particularly important in the discussion of the cardiovascular effects of cocaine and its effects on the respiratory system.

The action of cocaine on the nervous system can also cause seizures (convulsions), headaches, and strokes.

5.1 Seizures/Epilepsy

Seizures were one of the first known complications of cocaine use. They can occur in people known to have epilepsy, in otherwise normal people, and are commonly associated with death resulting from cocaine use. Increasing evidence suggests that women are more prone to develop seizures as a result of cocaine use than men.

In persons with a history of epilepsy, cocaine tends to induce their typical seizures. In these people, seizures can occur with low doses of cocaine and even after nasal injestion.

Cocaine also produces a direct convulsant effect that is evident in persons with no previous history of seizures. Reported cases have generally involved large doses, usually smoked or injected intravenously.

Seizures are a well recognized event associated with death resulting from cocaine use.[37] They have occurred after massive oral doses when condoms break in the digestive tract of persons smuggling cocaine (body-packing). Seizures can also result from large doses: smoked, taken intravenously, or even when snorted.

Interesting gender issues have arisen with respect to cocaine-related complications.[38] Animal studies show that females are more sensitive to some effects than males. Consistent with those findings, reports in humans indicate more females experience seizures during cocaine use, and at smaller doses. Yet chest pain is a more frequent complication for men. Further studies are required to confirm these findings and clarify their importance.

Cocaine related seizures have been reported to respond to diazepam (Valium^{R}) given by intravenous injection, but not always to other anticonvulsants.

5.2 Headaches

Headaches are a not uncommon complication of cocaine use.[39] Often no physical abnormalities are present and no lasting effects occur. For example, cocaine can trigger migraine headaches, and withdrawal can be associated with benign headaches. However, headaches can be a symptom of serious complications such as a stroke, so should not be ignored if they are severe or persistent.

5.3 Other Effects on the Nervous System

The effects of cocaine use on the nervous system can result in varying degrees of brain damage. Severe damage and even death, can result when a stroke occurs, also there is now evidence that brain damage can result from chronic use not associated with a specific event such as a stroke.

Cocaine-related stroke can result: when the blood supply to the brain is blocked (cerebral infarction), from bleeding into the brain (intracerebral hemorrhage) and from bleeding around the brain (subarachnoid hemorrhage). Reported cases of bleeding are frequently associated with an aneurysm or some other abnormality of a blood vessel.[40] The sudden increases in blood pressure produced by cocaine probably results in rupture of the weakened area.

Strokes have been reported after any route of cocaine administration, however in one study 94% followed use of crack.[41] They occur mostly in young people, and in first time users as well as chronic abusers.

Because of the various effects cocaine abuse can have on the nervous system, it has been hypothesized that it will produce some brain damage even in the absence of an event such as a stroke. A recent study of 20 heavy users of cocaine, supports this thesis.[42] They were more impaired than controls on a number of tests including those measuring: ability in arithmetic, concentration and memory, and nonverbal problem solving and abstracting ability. Further research is needed to confirm these findings.

6. PSYCHIATRIC EFFECTS

6.1 Symptoms and Diagnoses

Psychiatric symptoms of cocaine use vary widely between users and, over a period of time, in an individual user. Symptoms caused by cocaine use are frequently seen together with the effects of withdrawal; the picture is often further complicated by an underlying psychiatric illness. The psychiatric effects of cocaine are most commonly seen in chronic users, but can also occur in occasional users.

With chronic use, symptoms can progress from euphoria to dysphoria, then to paranoid psychosis. At first the user feels very good (euphoria), with continued use they can begin to feel increasingly uncomfortable (dysphoria), and finally become very suspicious and lose contact with reality (paranoid psychosis). These stages are common in chronic, heavy cocaine users, and often occur during an extended session ("run" "binge") where a large amount of drug is available.

The symptoms can be greatly intensified by the effects of withdrawal discussed above in the section on cocaine addiction. The dysphoria and loss of contact with reality become even more distressing when associated with drug craving, feelings of low energy and inability to experience pleasure that occur during withdrawal.

Patients with a number of psychiatric diagnoses tend to use cocaine. Those with depression may be attracted by its euphoric effects; those with bipolar disorders (manic-depression) may use it to enhance their highs and avoid their lows. Persons with the residual type of attention deficit disorder (hyperactivity) find it increases their attention span and decreased restlessness. These psychiatric findings are most common in chronic cocaine users, who also often have various personality disorders. In addition, cocaine use can induce panic attacks and up to one third of chronic adolescent users have evidence of an eating disorder.[43]

Treatment of major psychiatric symptoms during cocaine intoxication should be approached with caution since many of the standard drugs such as chorpromazine (Largactil^{R}) and trifluperazine (Stelazine^{R}) may worsen or precipitate cocaine seizures. Benzodiazepines such as diazepam (Valium^{R}) are generally adequate for the milder symptoms.

6.2 Depression

Symptoms of depression are commonly associated with cocaine use. They are a prominent feature of withdrawal; also, use of cocaine may be related to a pre-existing depressive illness.

A history of recent cocaine use will indicate that symptoms may be a result of withdrawal. Return to normal mood or significant reduction in the level of depression after four or five days of confirmed drug abstinence will then differentiate withdrawal symptoms from a major depressive disorder.[44]

Persons suffering from a severe depressive illness may unconsciously use (abuse) cocaine to treat their condition. Identification of these patients is important as treatment with antidepressant drugs should decrease the chance they will relapse to cocaine use.[45]

Antidepressant drugs, particularly desipramine (Pertofrane^{R}), have been used in the treatment of the craving associated with cocaine withdrawal. Although some promising results have been obtained these drugs are not yet a generally accepted treatment.[46]

6.3 Psychosis

Chronic, heavy cocaine users frequently present with psychosis: severe psychiatric symptoms indicating a clear loss of contact with reality.[47] Paranoia is often a prominent feature, with related suspiciousness and irrational fear that "someone is out to get them". Acute psychosis can develop during a cocaine "run", even in occasional users; a more lasting, and serious psychosis develops in some chronic users.

The acute psychosis is usually short lived, lasting only a matter of hours or days, if abstinence is ensured. In one group of 50 patients interviewed, 34 (68%) had developed transient paranoid episodes during their cocaine use, associated with 8 to 72 hour binges of drug taking.[48] The paranoid episodes typically began after an average of 34.7 months of cocaine use, so most were not occasional users. Patients often present with vivid visual, auditory and tactile hallucinations such as the delusion that insects are crawling under the skin.

In the longer lasting psychosis, patients are in a more deteriorated state and symptoms may persist for periods ranging from several days to a few weeks. This psychosis may be difficult to distinguish from paranoid schizophrenia except that it is relatively short term.

The violence commonly associated with cocaine use may, to a large part, be due to the illicit nature of the drug. However, the symptoms of suspiciousness and paranoia seen in cocaine users indicate that violence can also be a defensive reaction to irrational fear.[49]

7. OTHER MEDICAL EFFECTS

7.1 Immune SystemDepression

The effects of cocaine to depress the immune system are complex and not well understood. The subject has gained recent attention because of the high incidence of AIDS in poly drug users. Studies have linked a high risk of HIV infection to the sexual and injection behavior of cocaine users, but not to cocaine use itself.[50]

Cocaine has been shown to affect various components of the immune system. It acts directly on the immune cells and indirectly by altering the level of various hormones and nervous system chemicals that affect the immune system. Nutritional deficiencies resulting from cocaine's appetite suppression could contribute to immune depression.

In animal studies, cocaine has been shown to stimulate the function of immune cells such as T-lymphocytes and natural killer cells, and depress the function of others. However, even the "unnatural" stimulation may result in immune system depression. The results have not been consistent, and it is not yet clear if cellular function in humans is significantly altered.

The effects of cocaine on hormones and other chemicals that regulate the immune system are also very complex. It acts on neurotransmitters such as dopamine and serotonin as well as altering the levels of hormones such as beta-endorphin, ACTH, and corticosterone. These chemicals have multiple, inter-related effects on the immune response. The net outcome is difficult to assess because of its complexity and because of the effect of other factors such as psychological and social situation, including malnutrition.

The importance of the immune system depression caused by cocaine remains to be clarified. It could result in the development of various infections, and also contribute to the development of AIDS after infection with HIV.[51]

7.2 Allergic Reactions and Hypersensitivity

Sudden deaths associated with cocaine use may result from actual allergic reactions to the drug or to contaminants that are frequently present in "street" drugs.

Some hypersensitivity reactions, although not allergic in nature, may result from a deficiency of the enzyme pseudocholinesterase. The body requires this enzyme in order to break down cocaine and make it non-toxic. The affected user may suffer a serious overdose from what would be a usual dose of drug in a person with normal amounts of the enzyme.

7.3 Increase in Body Temperature (hyperpyrexia)

Hyperpyrexia, an extremely high body temperature, is a rarely reported complication of cocaine use.[52] When it does occur, a number of factors contribute. Increased activity causes greater heat production; constriction of blood vessels decreases heat loss; cocaine may also have an effect on the heat-regulating centres in the brain.[53]

The temperature increases can be sufficient to contribute to the development of seizures, life-threatening abnormal heart rhythms, and death.

7.4 Stomach and Intestines

Although cocaine is apparently taken orally (by mouth) quite commonly, little has been published about this route of administration. The lack of reports may result from the misconception that cocaine is broken down in the stomach and intestines and becomes inactive. In fact, oral use is at least as effective as the same intranasal dose. The subjective "highs" in humans have even been reported to be greater after oral use than with intranasal use.[54]

Oral use of cocaine has been reported to cause abdominal pain, nausea, vomiting and diarrhoea. These effects result from the reduced blood supply to the stomach and intestines (intestinal ischemia) caused by cocaine. Gangrene (death of the tissues) can result, particularly when very large doses of cocaine are released in the intestinal tract. An extreme example: when bags of cocaine swallowed by drug smugglers ("body packers" or "mules") accidentally rupture.

The action of cocaine on the stomach and intestines is not limited to oral use. Perforations (holes through the wall) of the stomach have been reported following crack smoking and equally severe intestinal complications have followed cocaine injection. These serious complications are always a possibility when a cocaine user has severe abdominal pain. Prompt surgical attention may be required as deaths have resulted.[55]

7.5 Liver

There now seems little doubt that cocaine, or one of its break down products (metabolites), can cause direct liver damage. Animal studies strongly support this conclusion as do an increasing number of reports in humans.[56]

Other causes of liver damage can occur in cocaine users. Direct drug-related causes: shock and low blood pressure, decreased oxygen supply, and very high temperatures. Indirect causes: viral hepatitis from injecting with unsterile equipment and, alcohol and other drugs taken in addition to cocaine.[57]

7.6 Overdose

Deaths related to cocaine use have increased significantly during the past decade as the use and abuse of cocaine has increased. Death is usually rapid and unpredictable; and has occurred with all routes of administration, and at a wide range of doses.

Death usually results from depression of vital brain centres which control respiration, leading to respiratory arrest. This being a more likely cause if a depressant drug such as heroin has also been taken. Seizures commonly occur prior to death. As outlined in the various sections above, death can result from events as varied as: abnormal rhythms of the heart, ruptured blood vessels, very high body temperature, and gangrene of the intestine.

Although most deaths have followed intravenous injection, they have also been reported following oral use, (the extreme cases resulting when bags swallowed by drug smugglers rupture in the stomach or intestines) and after smoking. Contrary to popular belief, deaths have also occurred in users who have snorted the drug.

The lethal dose of cocaine is not known, and is probably extremely variable, depending on tolerance and other drugs taken. Deaths have been reported after a single dose of a few hundred milligrams, yet in other cases a dose of several grams (several thousand milligrams) has not been fatal. Fatalities have been reported with very low doses: as low as 30 mg snorted and 20 mg injected. Virtually no dose, no matter how small, can be guaranteed safe.[58]

7.7 Sexual Function

Many users claim that cocaine is an aphrodisiac. No doubt, at low doses, delayed ejaculation and orgasm and mood elevation and heightened sensory awareness may produce an improved sexual experience.

On the other hand, men who have used cocaine for a long time, particularly at high doses, may have difficulty maintaining an erection and ejaculating, and many have frequent periods of complete sexual disinterest. Also, female users may have difficulties achieving orgasm.[59]

7.8 Muscle Wasting (rhabdomyolysis)

Several investigators implicate cocaine in the development of the muscle wasting disease rhabdomyolysis. It could be caused by inadequate oxygen supply resulting from constriction of blood vessels or be due to a direct toxic effect of cocaine on muscles.

In one group of 39 patients, a third also had acute kidney failure, often together with severe liver dysfunction and widespread blood clotting (disseminated intravascular coagulation). Six of the 13 patients with acute kidney failure died, adding yet another potentially fatal side effect to cocaine use.

7.9 Indirect Medical Effects

A number of indirect medical effects are associated with cocaine use. These effects generally relate to how the drug is taken or to social factors surrounding drug use.

Those who smoke cocaine, other than crack, usually prepare their own free base. The use of solvents in this process can result in explosions and fires leading to serious burns and other injuries.

Well known complications are associated with injecting illicit drugs with non-sterile equipment. Adulterants added to "street" drugs can be toxic and injecting incompletely dissolved substances can cause severe lung damage. Improperly sterilized equipment can cause infections (abscesses) at the site of injection, and by spread through the blood, infections in the lungs and especially on the valves of the heart (endocarditis). Other infections such as AIDS and hepatitis can also be transmitted in this way.

The exchange of sex for drugs or money to buy drugs is not an uncommon transaction. Apparently, this is a particularly common occurrence among young crack users, and has resulted in a high level of sexually transmitted diseases (STD's) including syphilis, AIDS, and hepatitis among this group.[60]

Despite the wide range of toxic effects of cocaine outlined in this review, apparently, many users still consider it a relatively safe, non-addictive drug.

This is unfortunate, since medically cocaine is not a safe drug. It is definitely addictive, causing both tolerance and withdrawal associated with very strong craving. Also, cocaine can cause serious damage to the heart and blood vessels, the lungs, the nervous system, and death from a variety of causes.

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